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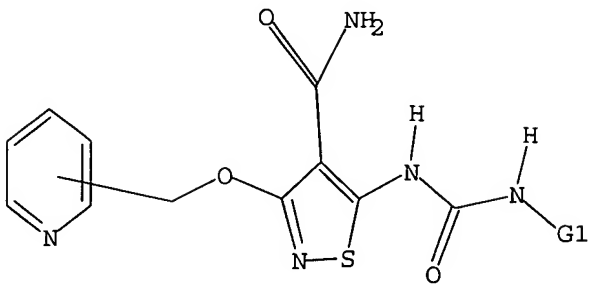


G1 Cb,Cy,Hy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l11 sub=l10 full
FULL SUBSET SEARCH INITIATED 16:05:12 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED - 44 TO ITERATE

100.0% PROCESSED 44 ITERATIONS 44 ANSWERS
SEARCH TIME: 00.00.01

L12 44 SEA SUB=L10 SSS FUL L11

=> s l12
L13 1 L12

=> d l13

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:609931 CAPLUS
DN 141:140432
TI Preparation of ureidoisothiazolecarboxamides as inhibitors of the transforming growth factor (TGF-β) signaling pathway.
IN Munchhof, Michael J.
PA Pfizer Inc, USA
SO U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004147574	A1	20040729	US 2004-765658	20040126
	WO 2004067530	A1	20040812	WO 2004-IB122	20040115

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

PRAI US 2003-442708P P 20030127

OS MARPAT 141:140432

=> s l8
L14 11 L8

=> d l14 1-11 ibib abs

L14 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995713 CAPLUS
DOCUMENT NUMBER: 141:420610
TITLE: Surface receptor complexes as biomarkers of disease and for determination of treatment with dimer-acting drugs
INVENTOR(S): Chan-Hui, Po-Ying; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 67 pp., Cont.-in-part of U.S. Ser. No. 623,057.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229293	A1	20041118	US 2004-812619	20040330
US 2003013126	A1	20030116	US 2002-154042	20020521
US 2004126818	A1	20040701	US 2003-623057	20030717
US 2004197835	A1	20041007	US 2004-830543	20040422
PRIORITY APPLN. INFO.:			US 2002-154042 A2	20020521
			US 2002-398724P P	20020725
			US 2003-459888P P	20030401
			US 2003-623057 A2	20030717
			US 2003-494482P P	20030811
			US 2003-508034P P	20031001
			US 2003-512941P P	20031020
			US 2003-523258P P	20031118
			US 2001-292548P P	20010521
			US 2001-334901P P	20011024

AB The invention is directed to a new class of biomarker in patient samples comprising dimers of cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. of one or more dimers of cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a cancer in a specimen from an individual by correlating measurements of amts. of one or more dimers of cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a cancer, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. having releasable mol. tags that are specific for multiple components of one or more types of receptor dimers. After binding, mol. tags are released and separated from the assay mixture for anal.

L14 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965067 CAPLUS
DOCUMENT NUMBER: 141:406039
TITLE: Combinations for the treatment of diseases involving cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis
INVENTOR(S): Hilberg, Frank; Solca, Flavio; Stefanic, Martin Friedrich; Baum, Anke; Munzert, Gerd; Van Meel, Jacobus C. A.
PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.
SOURCE: PCT Int. Appl., 101 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096224	A2	20041111	WO 2004-EP4363	20040424
WO 2004096224	A3	20041216		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1473043	A1	20041103	EP 2003-9587	20030429

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:	EP 2003-9587	A	20030429
	EP 2004-508	A	20040113
	EP 2004-1171	A	20040121

AB The present invention relates to a pharmaceutical combination for the treatment of diseases which involves cell proliferation, migration or apoptosis of myeloma cells, or angiogenesis. The invention also relates to a method for the treatment of said diseases, comprising co-administration of effective amts. of specific active compds. and/or co-treatment with radiation therapy, in a ratio which provides an additive and synergistic effect, and to the combined use of these specific compds. and/or radiotherapy for the manufacture of corresponding pharmaceutical combination prepns. The pharmaceutical combination can include selected protein tyrosine kinase receptor antagonists and further chemotherapeutic or naturally occurring semisynthetic or synthetic agents.

L14 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:905883 CAPLUS
DOCUMENT NUMBER: 141:361107
TITLE: Methods for the detection of cell surface receptor complexes as cancer biomarkers and therapeutic effectiveness of cleavage thereof
INVENTOR(S): Chan-Hui, Po-Ying; Salimi-Moosavi, Hossein; Shi, Yining; Singh, Sharat; Dua, Rajiv; Mukherjee, Ali; Pidaparthi, Sailaja
PATENT ASSIGNEE(S): Aclara Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 29
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092353	A2	20041028	WO 2004-US9717	20040330

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

US 2004126818	A1	20040701	US 2003-623057		20030717
PRIORITY APPLN. INFO.:			US 2003-459888P	P	20030401
			US 2003-623057	A	20030717
			US 2003-494482P	P	20030811
			US 2003-508034P	P	20031001
			US 2003-512941P	P	20031020
			US 2003-523258P	P	20031118
			US 2002-398724P	P	20020725

AB The invention is directed to a new class of biomarker in patient samples comprising dimers of cell surface membrane receptors. In one aspect, the invention includes a method of determining the status of a disease or healthful condition by correlating such condition to amts. of one or more dimers of cell surface membrane receptors measured directly in a patient sample, in particular a fixed tissue sample. In another aspect, the invention includes a method of determining a status of a cancer in a specimen from an individual by correlating measurements of amts. of one or more dimers of cell surface membrane receptors in cells of the specimen to such status, including presence or absence of a pre-cancerous state, presence or absence of a cancerous state, prognosis of a cancer, or responsiveness to treatment. Preferably, methods of the invention are implemented by using sets of binding compds. having releasable mol. tags that are specific for multiple components of one or more types of receptor dimers. After binding, mol. tags are release and separated from the assay mixture for anal.

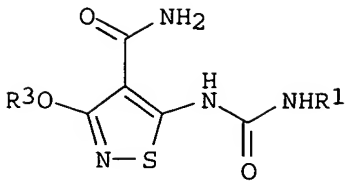
L14 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:609931 CAPLUS
DOCUMENT NUMBER: 141:140432
TITLE: Preparation of ureidoisothiazolecarboxamides as inhibitors of the transforming growth factor (TGF-β) signaling pathway.
INVENTOR(S): Munchhof, Michael J.
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

same

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004147574	A1	20040729	US 2004-765658	20040126
WO 2004067530	A1	20040812	WO 2004-IB122	20040115

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
MZ, MZ, NA, NI

PRIORITY APPLN. INFO.: US 2003-442708P P 20030127
OTHER SOURCE(S): MARPAT 141:140432
GI



I

AB Title compds. [I; R1 = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heterocyclyl(alkyl); R3 = (substituted) heteroaryl(alkyl)], were prepared Thus, 5-[3-(3,5-dimethoxybenzyl)ureido]-3-(pyridin-3-ylmethoxy)isothiazole-4-carboxamide (preparation outlined) inhibited TGF-β type II receptor kinase activity with IC50 = 0.353 μM. I are useful in the treatment of TGF-related disease states including hyperproliferative disorders and fibrotic diseases.

L14 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182702 CAPLUS
DOCUMENT NUMBER: 140:229421
TITLE: Combination therapy for hyperproliferative diseases by coadministration of isothiazole derivative and other antitumor agents
INVENTOR(S): Beebe, Jean Saccuzzo; Ferrante, Karen Jean; Jani, Jitesh Pranlal; Schaeffer, Tracey Lee; Healey, Diane Ingeborg; O'Leary, James John
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017964	A1	20040304	WO 2003-IB3550	20030807

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-404461P P 20020819
OTHER SOURCE(S): MARPAT 140:229421
AB The invention provides a method of treating hyperproliferative diseases, such as cancer, comprising the step of adminestering to a mammal in need of such treatment, either simultaneously or sequentially, (i) a therapeutically effective amount of a taxane derivative, a platinum coordination complex selected from the group consisting of carboplatin, tetraplatin, and topotecan, a nucleoside analog selected from the group consisting of gemcitabine hydrochloride and 5-FU, an anthracycline, a topoisomerase selected from the group consisting of etoposide, teniposide, amsacrine, topotecan and CamptosarU, an aromatase inhibitor; and (ii) a therapeutically effective amount of an isothiazole derivative The combinations of the invention may optionally include an anti-hypertensive agent. This invention also relates to pharmaceutical compns. useful in the treatment

of hyperproliferative diseases in mammals, containing such combinations. The invention also relates to kits having a first compartment with a compound of formula and a second compartment containing a taxane derivative, a platinum coordination complex, a nucleoside analog, an anthracycline, a topoisomerase inhibitor, or an aromatase inhibitor and a third compartment containing an anti-hypersensitive agent.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:182368 CAPLUS
DOCUMENT NUMBER: 140:229401
TITLE: Three hybrid assay system for isolating ligand-binding polypeptides and for isolating small mol. ligands
INVENTOR(S): Come, Jon H.; Becker, Frank; Kley, Nikolai A.; Reichel, Christoph
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 238 pp., Cont.-in-part of U.S. Ser. No. 91,177.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004043388	A1	20040304	US 2002-234985		20020903
US 2003165873	A1	20030904	US 2002-91177		20020304
US 2004266854	A1	20041230	US 2004-820453		20040407
PRIORITY APPLN. INFO.:			US 2001-272932P	P	20010302
			US 2001-278233P	P	20010323
			US 2001-329437P	P	20011015
			US 2002-91177	A2	20020304
			US 2001-336962P	P	20011203
			WO 2002-US6677	A2	20020304
			US 2002-234985	A2	20020903
			WO 2002-US33052	A2	20021015
			US 2003-460921P	P	20030407
			US 2003-531872P	P	20031223

AB The invention provides compns. and methods for isolating ligand-binding polypeptides for a user-specified ligand, and for isolating small mol. ligands for a user-specified target polypeptide using an improved class of hybrid ligand compds. Preparation of compds., e.g a methotrexate moiety linked by a polyethylene gycol moiety to dexamethasone, is described.

L14 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:885654 CAPLUS
DOCUMENT NUMBER: 140:138923
TITLE: Pharmacological Characterization of CP-547,632, a Novel Vascular Endothelial Growth Factor Receptor-2 Tyrosine Kinase Inhibitor for Cancer Therapy
AUTHOR(S): Beebe, Jean S.; Jani, Jitesh P.; Knauth, Elisabeth; Goodwin, Peter; Higdon, Carla; Rossi, Ann Marie; Emerson, Erling; Finkelstein, Martin; Floyd, Eugenia; Harriman, Shawn; Atherton, Jim; Hillerman, Steve; Soderstrom, Cathy; Kou, Kou; Gant, Tom; Noe, Mark C.; Foster, Barb; Rastinejad, Farzan; Marx, Matthew A.; Schaeffer, Tracey; Whalen, Pamela M.; Roberts, W. Gregory
CORPORATE SOURCE: Cancer Drug Discovery, Pfizer Global Research and Development, Groton, CT, 06340, USA
SOURCE: Cancer Research (2003), 63(21), 7301-7309

CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Signaling through vascular endothelial growth factor (VEGF) receptors (VEGFRs) is a key pathway initiating endothelial cell proliferation and migration resulting in angiogenesis, a requirement for human tumor growth and metastasis. Abrogation of signaling through VEGFR by a variety of approaches has been demonstrated to inhibit angiogenesis and tumor growth. Small mol. inhibitors of VEGFR tyrosine kinase have been shown to inhibit angiogenesis, inhibit tumor growth, and prevent metastases. Our goal was to discover and characterize an p.o. active VEGFR-2 small mol. inhibitor. A novel isothiazole, CP-547,632, was identified as a potent inhibitor of the VEGFR-2 and basic fibroblast growth factor (FGF kinases) (IC50 = 11 and 9 nM, resp.). It is selective relative to epidermal growth factor receptor, platelet-derived growth factor β, and other related TKs. It also inhibits VEGF-stimulated autophosphorylation of VEGFR-2 in a whole cell assay with an IC50 value of 6 nM. After oral administration of CP-547,632 to mice bearing NIH3T3/H-ras tumors, VEGFR-2 phosphorylation in tumors was inhibited in a dose-dependent fashion (EC50 = 590 ng/mL). These plasma concns. correlated well with the observed concns. of the compound necessary to inhibit VEGF-induced corneal angiogenesis in BALB/c mice. A sponge angiogenesis assay was used to directly compare the inhibitory activities of CP-547,632 against FGF receptor 2 or VEGFR-2; this compound potently inhibits both basic FGF and VEGF-induced angiogenesis in vivo. The antitumor efficacy of this agent was evaluated after once daily p.o. administration to athymic mice bearing human xenografts and resulted in as much as 85% tumor growth inhibition. CP-547,632 is a well-tolerated, orally-bioavailable inhibitor presently under clin. investigation for the treatment of human malignancies.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:719299 CAPLUS
DOCUMENT NUMBER: 139:240339
TITLE: Antitumor agent comprising combination of sulfonamide-containing heterocyclic compound with angiogenesis inhibitor
INVENTOR(S): Wakabayashi, Toshiaki; Ono, Naoto; Semba, Taro; Haneda, Toru
PATENT ASSIGNEE(S): Eisai Co., Ltd., Japan
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

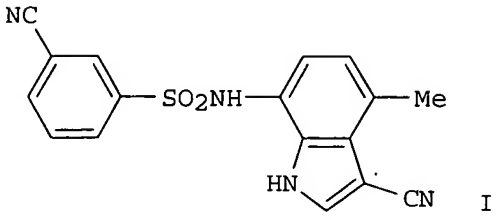
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074045	A1	20030912	WO 2003-JP2492	20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1481678	A1	20041201	EP 2003-743594	20030304

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.: JP 2002-59471 A 20020305
WO 2003-JP2492 W 20030304

OTHER SOURCE(S): MARPAT 139:240339

GI



I

AB It is intended to provide compns. and kits for treating tumor whereby the angiogenesis inhibitory activity and the antitumor activity of a sulfonamide-containing heterocyclic compound represented by the following formula (I) can be more effectively exerted. By combining with a VEGF inhibitor or an FGF inhibitor, the sulfonamide-containing heterocyclic compound can be effectively employed in treating cancer.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:428887 CAPLUS
DOCUMENT NUMBER: 137:24295
TITLE: Salts of an isothiazole-4-carboxamide derivative, namely 3-(4-bromo-2,6-difluorobenzyloxy)-5-[3-(4-pyrrolidin-1-ylbutyl)ureido]isothiazole-4-carboxylic acid amide, and their use as anti-hyperproliferation agents
INVENTOR(S): Gant, Thomas G.; Williams, Glenn Robert
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044158	A1	20020606	WO 2001-IB2193	20011119
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2430065	AA	20020606	CA 2001-2430065	20011119
AU 2002014204	A5	20020611	AU 2002-14204	20011119
EP 1337521	A1	20030827	EP 2001-982663	20011119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001015621	A	20030902	BR 2001-15621	20011119

EE 200300247	A	20031015	EE 2003-247		20011119
JP 2004514714	T2	20040520	JP 2002-546528		20011119
NZ 525788	A	20041126	NZ 2001-525788		20011119
US 2002151573	A1	20021017	US 2001-993640		20011127
US 6831091	B2	20041214			
BG 107752	A	20040130	BG 2003-107752		20030422
ZA 2003003341	A	20040430	ZA 2003-3341		20030430
HR 2003000408	A1	20030831	HR 2003-408		20030520
NO 2003002388	A	20030718	NO 2003-2388		20030527
PRIORITY APPLN. INFO.:			US 2000-253513P	P	20001128
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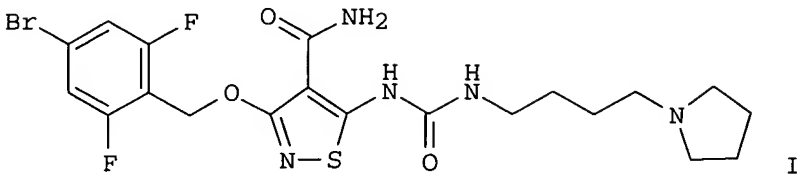

I

AB The invention relates to the hydrochloride, hydrobromide, hemi-citrate, acetate, p-tosylate, L-tartrate, hemi-succinate, and mesylate salt forms of 3-(4-bromo-2,6-difluoro-benzyloxy)-5-[3-(4-pyrrolidin-1-ylbutyl)ureido]isothiazole-4-carboxylic acid amide (I). These salts of I are useful in the treatment of various hyperproliferative diseases, including cancers (no data). The invention also relates to pharmaceutical compns. containing these salts. The invention further relates to methods of treating hyperproliferative diseases, such as cancers, in mammals, especially humans, by administering the above salts, and to methods of preparing the crystal forms of the salts. For instance, I was dissolved in refluxing EtOH, and the solution was cooled to ambient temperature, treated with 1 equiv HCl (1.0M in Et2O), heated to 50°, and cooled at room temperature for 3 days to give I.HCl in 82% yield. The advantageous properties of all the salts are described in detail; e.g., I.HCl showed high crystallinity, was hygroscopically stable, and had a low tendency for concentrated aqueous solns. to form viscous mixts. on standing. Characterizing X-ray powder diffraction spectra are given for I and salts, both as tables and graphical figures.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:784087 CAPLUS
DOCUMENT NUMBER: 132:22961
TITLE: Preparation of isothiazolamide urea derivatives as anticancer agents
INVENTOR(S): Larson, Eric Robert; Noe, Mark Carl; Gant, Thomas George
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9962890	A1	19991209	WO 1999-IB797	19990503

Submitted w/IDS

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2333703	AA	19991209	CA 1999-2333703	19990503
CA 2475113	AA	19991209	CA 1999-2475113	19990503
AU 9933421	A1	19991220	AU 1999-33421	19990503
BR 9910900	A	20010213	BR 1999-10900	19990503
EP 1084114	A1	20010321	EP 1999-914724	19990503
EP 1084114	B1	20040908		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 200003478	T2	20010321	TR 2000-200003478	19990503
JP 2002517384	T2	20020618	JP 2000-552102	19990503
NZ 507009	A	20031128	NZ 1999-507009	19990503
AT 275553	E	20040915	AT 1999-914724	19990503
US 6235764	B1	20010522	US 1999-316837	19990521
TW 561154	B	20031111	TW 1999-88108991	19990531
ZA 9903752	A	20001204	ZA 1999-3752	19990603
BG 104998	A	20010731	BG 2000-104998	20001128
NO 2000006071	A	20001130	NO 2000-6071	20001130
HR 2000000835	A1	20011231	HR 2000-835	20001204
US 2001020034	A1	20010906	US 2001-803296	20010309
US 6548526	B2	20030415		
US 2003149048	A1	20030807	US 2003-357093	20030203
JP 2005002122	A2	20050106	JP 2004-209396	20040716

PRIORITY APPLN. INFO.:

US 1998-87963P	P	19980604
CA 1999-2333703	A3	19990503
JP 2000-552102	A3	19990503
WO 1999-IB797	W	19990503
US 1999-316837	A3	19990521
US 2001-803296	A3	20010309

OTHER SOURCE(S): MARPAT 132:22961

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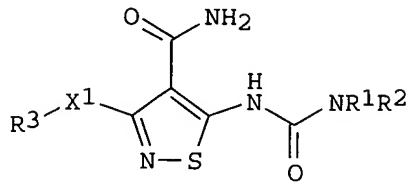

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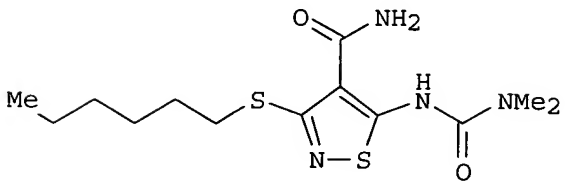

II

AB Title compds. (I) [X1 = O or S; R1 = H, (un)substituted alkyl, alkenyl, alkynyl, acyl, (CH2)t(hetero)aryl, C(O)(CH2)t(hetero)aryl, etc.; t = 0-5; R2 = R1, SO2(CH2)t(hetero)aryl, etc.; or R1 and R2 taken together with the

attached N = 4-10 membered (un)substituted poly- or monocyclic ring or 5-10 membered (un)substituted heteroaryl ring; R3 = H, (un)substituted alkyl, alkenyl, alkynyl, (CH2)t(hetero)aryl, etc.] were prepared for use in the treatment of hyperproliferative disorders, such as cancer. Thus, 3-(4-cyano-3-mercaptoisothiazol-5-yl)-1,1-dimethylurea (preparation given) was alkylated with 1-iodohexane (51%) and the product treated with concentrated H2SO4 to yield the isothiazolamide (II) (78%). I are inhibitors of receptor tyrosine kinases and bind to or modulate the KDR/FLK-1 receptor (no data) and may be used to treat disorders related to vasculogenesis or angiogenesis.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1978:50846 CAPLUS
DOCUMENT NUMBER: 88:50846
TITLE: 3-Alkoxyisothiazole derivatives as herbicides
INVENTOR(S): Gibbons, Loren Kenneth
PATENT ASSIGNEE(S): FMC Corp., USA
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4059433	A	19771122	US 1976-697457	19760618

PRIORITY APPLN. INFO.: US 1976-697457 A 19760618

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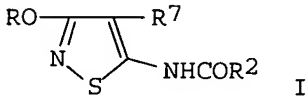

I

AB Alkoxyisothiazoles I (R = C1-5 alkyl; R1 = CN, CONH2; R2 = C1-5 alkyl, NR3R4; R3 = C1-5 alkyl, R4 = H, C1-5 alkyl) were prepared Thus CH2(CN)2 was treated with KBr to give CBr2(CN)2.KBr, which was treated with KCN to give KC(CN)3. Ethanolysis of KC(CN)3 gave EtOC(NH2):C(CN)2, which on treatment with H2S gave EtOC(NH2):C(CN)CSNH2. Treatment of the thioamide with H2O2 gave 5-amino-4-cyano-3-ethoxyisothiazole, which was treated with MeNCO to give I (R = Et, R1 = CN, R2 = NHMe). At 8.96 kg/ha post-emergence I (R = Et, R1 = CN, R2 = NHMe) gave 100% control of lettuce, mustard, or crabgrass in corn.

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E2            1     MUNCHHOF MARTHA G/AU
E3           12 --> MUNCHHOF MICHAEL J/AU
E4           11     MUNCHHOF MICHAEL JOHN/AU
E5            1     MUNCHHOFF MIKE/AU
E6            1     MUNCHI M Z/AU
E7            1     MUNCHIN JAY Z/AU
E8            2     MUNCHINGER R/AU
E9            2     MUNCHMEYER A/AU
E10           4     MUNCHMEYER F C/AU
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E13           3     MUNCHMEYER GEORG/AU
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E16           1     MUNCHMEYER RICKARD/AU
E17           1     MUNCHMEYER TED/AU
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E20           1     MUNCHMEYER W/AU
E21           7     MUNCHMEYER WOLF/AU
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E25           1     MUNCHOW E B/AU

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L2             2 FOCUS L1 1-

=> DIS L2 1- ALL
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):Y

L2   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2005 ACS on STN
AN   2004:609931  CAPLUS
DN   141:140432
ED   Entered STN:  30 Jul 2004
TI   Preparation of ureidoisothiazolecarboxamides as inhibitors of
     the transforming growth factor (TGF-β) signaling pathway.
IN   Munchhof, Michael J.
PA   Pfizer Inc, USA
SO   U.S. Pat. Appl. Publ., 15 pp.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  C07D275-02
     ICS  A61K031-42
NCL  514376000; 548213000; 514342000; 546271100
CC   28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
     Section cross-reference(s): 1
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI US 2004147574 A1 20040729 US 2004-765658 20040126
WO 2004067530 A1 20040812 WO 2004-IB122 20040115
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI
PRAI US 2003-442708P P 20030127
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2004147574	ICM	C07D275-02
	ICS	A61K031-42
	NCL	514376000; 548213000; 514342000; 546271100

OS MARPAT 141:140432
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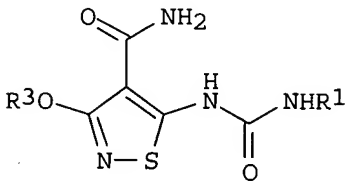

I

AB Title compds. [I; R1 = (substituted) alkyl, cycloalkyl(alkyl), aryl(alkyl), heterocyclyl(alkyl); R3 = (substituted) heteroaryl(alkyl)], were prepared Thus, 5-[3-(3,5-dimethoxybenzyl)ureido]-3-(pyridin-3-ylmethoxy)**isothiazole**-4-carboxamide (preparation outlined) inhibited TGF-β type II receptor kinase activity with IC50 = 0.353 μM. I are useful in the treatment of TGF-related disease states including hyperproliferative disorders and fibrotic diseases.

ST **isothiazolecarboxamide** prepn transforming growth factor signaling pathway inhibitor; hyperproliferative disorder fibrotic disease treatment **pyridinylmethoxyureidoisothiazolecarboxamide** prepn; TGF related disease treatment **ureidoisothiazolecarboxamide** pyridinylmethoxy prepn

IT Antitumor agents
Human
(preparation of **isothiazolecarboxamides** as inhibitors of the TGF-β signaling pathway)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of **isothiazolecarboxamides** as inhibitors of the TGF-β signaling pathway)

IT Fibrosis
Neoplasm
(treatment; preparation of **isothiazolecarboxamides** as inhibitors of the TGF-β signaling pathway)

IT Transforming growth factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-; preparation of **isothiazolecarboxamides** as inhibitors of the TGF-β signaling pathway)

IT 727359-37-7P 727359-38-8P 727359-39-9P 727359-40-2P 727359-41-3P
727359-42-4P 727359-43-5P 727359-44-6P 727359-45-7P 727359-46-8P
727359-47-9P 727359-48-0P 727359-49-1P 727359-50-4P 727359-51-5P
727359-52-6P 727359-53-7P 727359-54-8P 727359-55-9P 727359-56-0P
727359-57-1P 727359-58-2P 727359-59-3P 727359-60-6P 727359-61-7P
727359-62-8P 727359-63-9P 727359-64-0P 727359-65-1P 727359-66-2P

727359-67-3P 727359-68-4P 727359-69-5P 727359-70-8P 727359-71-9P
727359-72-0P 727359-73-1P 727359-74-2P 727359-75-3P 727359-76-4P
727359-77-5P 727359-78-6P 727359-79-7P 727359-80-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; preparation of **isothiazolecarboxamides** as inhibitors of the TGF-β signaling pathway)

IT 252004-30-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of **isothiazolecarboxamides** as inhibitors of the TGF-β signaling pathway)

L2 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:942789 CAPLUS
DN 138:24721
ED Entered STN: 12 Dec 2002
TI Preparation of thienopyrimidines and thienopyridines as anticancer agents
IN **Munchhof, Michael John**; Sobolov-Jaynes, Susan Beth; Marx, Matthew Arnold
PA Pfizer Inc., USA
SO U.S., 37 pp., Cont.-in-part of Appl. No. PCT/IB98/1691.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-44
ICS A61K031-517; C07D239-70; C07D515-02
NCL 514301000; 514258100; 544253000; 546114000
CC 28-16 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6492383	B1	20021210	US 2000-502129	20000210
	WO 9924440	A1	19990520	WO 1998-IB1691	19981022
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003162795	A1	20030828	US 2002-244324	20020916
PRAI	WO 1998-IB1691	A2	19981022		
	US 2001-65097P	P	20011111		
	US 1997-65097P	P	19971111		
	US 2000-502129	A1	20000210		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6492383	ICM	A61K031-44
	ICS	A61K031-517; C07D239-70; C07D515-02
	NCL	514301000; 514258100; 544253000; 546114000
US 6492383	ECLA	C07D495/04+333B+239B; C07D495/04+333B+221B
WO 9924440	ECLA	C07D495/04+333B+221B; C07D495/04+333B+239B

OS MARPAT 138:24721
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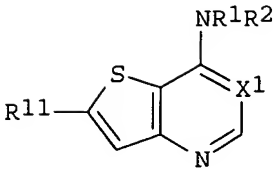

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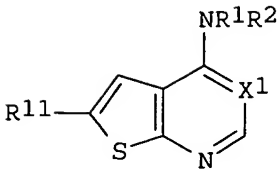

II

AB The title compds. [I and II; X1 = CH; R1 = H, alkyl, C(O)alkyl; R2 = aryl, heterocyclic; R11 = H, alkyl, C(O)NR6R9, etc.; R6 = H, alkyl, etc.; R9 = H, alkyl, etc.] and analogs useful for treating hyperproliferative disorders, were prepared E.g., a multi-step synthesis of I [X1 = N; R1 = indol-5-yl; R2 = H; R11 = Br], was given. Compds. I are effective at 0.2-2.5 g/day for a 70 kg human.